

**REMARKS**

Upon entry of the Amendment above, claims 1-18, 21-33, 35-36, 43-46, 48-53, 58-59, 61-63 and 68 will be pending in this application. By this amendment, claims 1, 21, 22, 27 and 35 have been amended, and claims 19, 20, 34, 37-42, 47, 54-57, 60, 64-67 and 69 have been cancelled. No new matter has been added as a result of the Amendment above.

Reconsideration of the merits of the application is respectfully requested in light of the Amendment above and the Remarks that follow.

**Reza (U.S. 2002/00116030)**

Claims 1-13, 19-21, 23-24, 27-31, 34-35, 40, 42, 47, 55, 57, and 59-60 have been rejected under 35 USC § 102(b) as allegedly being anticipated by, or in the alternative, under 35 USC § 103(a) as allegedly obvious over U.S. Pre-Grant Published Patent Application No. 2002/0116030 ("Reza"). Applicant respectfully traverses the rejection to the extent it is maintained.

According to the Office Action, Reza discloses stimulation of sympathetic neurons in patients suffering from or at risk of disorders such as asthma, pancreatitis, inflammatory bowel disease, and others that are mediated by an inflammatory cytokine cascade. Thus, according to the Office Action, Reza inherently teaches inhibition of release of a proinflammatory mediator in a subject suffering from, or at risk of, a disease or disorder mediated by a pro-inflammatory mediator.

Applicant asserts that Reza fails to disclose stimulation of a sympathetic neuron in a subject suffering from or at risk of one of the diseases or disorders specifically recited in independent claims 1 or 27 as amended. As such, Reza does not anticipate independent claims 1 or 27, or any of their dependent claims.

Applicant further asserts that one of skill in the art would not be lead to stimulate a sympathetic neuron to reduce inflammation in a subject suffering from or at risk of a disease or disorder specifically recited in independent claims 1 or 27 as amended. Reza is devoid of any teaching that stimulation of a neuron of the sympathetic system can result in inhibition of release of a pro-inflammatory mediator. While Reza does disclose that stimulation of the sympathetic

chain or ganglia may be useful for treating diseases that may be associated with inflammation, Rezai teaches that such stimulation would be useful for addressing the mechanical aspects of such diseases. For example, Rezai teaches that stimulation of the lower cervical and upper thoracic sympathetic ganglia may be helpful for treating bronchospasms associated with asthma "by controlling the contraction of smooth muscles of the airways."<sup>1</sup> By way of further example, Rezai teaches that stimulation of certain sympathetic ganglia may be useful for treating inflammatory bowel disease and other diseases by "affecting motility of the gastrointestinal system."<sup>2</sup> Nothing in Rezai would lead on of skill in the art to treat inflammatory aspects of a disease through sympathetic stimulation. Further, nothing in Rezai would lead one of skill in the art to stimulate a sympathetic neuron to reduce inflammation in a subject suffering from or at risk of one or more diseases specifically recited in claims 1 or 27 as amended. Accordingly, Rezai does not render obvious independent claims 1 or 27, or any of their dependent claims.

Withdrawal of this rejection is respectfully requested.

**Rezai in view of Tracey (U.S. 6,610,713)**

Claims 14–18, 22, 26, 33, 36–39, 41, 43–46, 48–54, 56, 58, and 61–69 have been rejected under 35 USC § 103(a) as allegedly being as unpatentable over Rezai in view of U.S. Patent No. 6,610,713 ("Tracey"). Applicant respectfully traverses the rejection to the extent it is maintained.

Tracey fails to overcome the deficiencies of Rezai discussed above with respect to independent claims 1 and 27, and thus the combination of Tracey and Rezai does not render dependent claims 14–18, 22, 26, 33, 36–39, 41, 43–46, 48–54, 56, 58, and 61–69 obvious. In fact, the combination of Tracey and Rezai would teach away from independent claims 1 and 27, and thus dependent claims 14–18, 22, 26, 33, 36–39, 41, 43–46, 48–54, 56, 58, and 61–69. As stated above, Rezai does not recognize that stimulation of the sympathetic system (or a neuron thereof) would produce an anti-inflammatory effect, while Tracey teaches that stimulation of the parasympathetic system (or a neuron thereof) results in an anti-inflammatory response. The

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<sup>1</sup> Paragraph 61, emphasis added.

<sup>2</sup> Paragraph 60, emphasis added.

sympathetic (fight or flight) and parasympathetic (rest and digest) nervous systems generally act in opposing fashion. Stimulation of the sympathetic system (or a neuron thereof) would be expected to produce a result that is vastly different from stimulation of the parasympathetic system (or a neuron thereof). One of skill in the art would not look to stimulating a neuron of the sympathetic system to effectuate a physiological change similar to one shown to occur when stimulating the parasympathetic system. Because of the antagonist nature of these two systems, one would not have expected that stimulating a neuron of the sympathetic system would result in inhibition or the release of a pro-inflammatory mediator or inhibition of an inflammatory cytokine cascade in a manner similar to the parasympathetic system. In fact, one would have expected an *increased* inflammatory response if reviewing the disclosure of Rezai in light of Tracey. Accordingly, the combined disclosures of Rezai and Tracey *teach away* from any and all claims of the present application. Accordingly the combination of Rezai and Tracey does not render obvious claims 14–18, 22, 26, 33, 36–39, 41, 43–46, 48–54, 56, 58, and 61–69.

Withdrawal of this rejection is respectfully requested.

**Rezai re claims 25 and 32**

Claims 25 and 32 have been rejected under 35 USC § 103(a) as allegedly being as unpatentable over Rezai. According to the Office Action, even though Rezai does not disclose direct stimulation of a peripheral tissue or organ served by the splenic nerve, it would have been obvious to apply such stimulation. Applicant traverses the rejection to the extent it is maintained.

For at least the reasons discussed above with regard to independent claims 1 and 27, Rezai does not render claims 25 and 32 obvious.

In addition, Rezai teaches away from direct stimulation of a peripheral tissue or organ served by the splenic nerve. Rezai teaches stimulation along the sympathetic chain<sup>1</sup> or a

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<sup>1</sup> At paragraph 26, Rezai defines the sympathetic chain as the cord that connects the ganglia. This definition is consistent with Figure 1 of the Rezai publication.

sympathetic ganglia along the sympathetic chain.<sup>4</sup> Stimulation of the sympathetic ganglia along the sympathetic chain (as opposed to closer to the end organ) produces "wide and far-reaching effects," which according to Rezai is desirable.<sup>5</sup> Applicant respectfully asserts that one of skill in the art would not have considered direct stimulation of a peripheral tissue or organ served by the splenic nerve an obvious choice upon reading the Rezai disclosure.

Withdrawal of this rejection is respectfully requested.

### Provisional Rejections

Claims 1-69 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-129 of copending Application Serial No. 10/820,677 now Publication No. 2005/0075701 ("Shafer").

As this rejection is provisional, Applicant will address this double patenting rejection, if appropriate, upon allowance of the claims presented herein.

In view of the foregoing amendments, Applicants respectfully request reconsideration and allowance of the claims as all rejections have been overcome. Notice to this effect is kindly requested.

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<sup>4</sup> See, e.g., paragraphs 4, 11, 14, 16, 26, where Rezai repeatedly discusses stimulation of a ganglion along the sympathetic chain. Stimulation of ganglia along the sympathetic chain is touted by Rezai as being desirable because wide and far-reaching effects can be attained. See paragraph 26, last sentence.


<sup>5</sup> Paragraph 26, last sentence.

The Examiner is respectfully requested to contact the undersigned by telephone at 763.505.0003 or by E-mail at [mary.p.bauman@medtronic.com](mailto:mary.p.bauman@medtronic.com) with any questions or comments.

Please grant any extension of time, if necessary for entry of this paper, and charge any fee due for such extension or any other fee required in connection with this paper to Deposit Account No. 13-2546.

Respectfully submitted,

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